

Characterization and Modulation of PI3K-Akt Signaling Following Contusive SCI

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Abstract

Spinal cord injury (SCI) is devastating, with most injuries being contusive/compressive injuries at the cervical spinal level. There are two mechanisms of damage after acute contusive SCI: a primary mechanical insult to the cord, and secondary injury induced by many biological events, including inflammation and signal-mediated cell death. The extent of tissue damage correlates with functional loss after SCI, therefore it is critical to protect neural tissue for preservation of functional ability. Focusing on cellular signaling events following SCI is a promising direction of investigation, as modulation of such pathways can promote neuroprotection or regeneration following injury. Two particular signaling pathways have been highlighted as mediators of cellular survival post-central nervous system (CNS) injury, the MEK-Erk and PI3K-Akt pathways. Reducing Erk activity has been shown to promote neuroprotection and reduced reactive gliosis, while reduction of PI3K-Akt signaling likely results in initiation of cellular death. Recent studies have demonstrated promotion of regrowth of adult corticospinal (CST) neurons and protection of motor neuron atrophy by disinhibition of PI3K via PTEN deletion or knock-down in these cells. Understanding the signal pathways and mechanisms involved in different cell types, when such response occurs, and the potential interaction between pathways is essential for maximizing development of optimal approaches to treatment following SCI. This study highlights PI3K-Akt signaling involvement following injury, with future directions aimed at better understanding this pathway for targeting therapies to mediate anatomical and functional preservation and recovery following SCI.